

R Bruce Wallace

JAN - 3 1982

DNA as mutagen

How thoughtful of you to recall what I wrote 22 years ago! The deeper my regrets that my calendar is fully booked for the time of your meeting. If it should open up unexpectedly I will write back to you.

You may recall how Dobzhansky characterized the pneumococcus transformation as a "directed mutation" even before Avery & co. characterized DNA there.

This may seem a semantic nicety but Avery (and Harriett Ephrussi) were informed by it in such a way that they avoided doing or interpreting multi-marker recombination expts. in a simple, straightforward way; and this was left to Rollin Hotchkiss some years later.

Best wishes
John Peck

when a strain lives, one of the phases is selected and displaces the other. The unique feature is the convergence observed in the rough phase resulting in an apparent loss of the distinctions between the types. The mutations from smooth to rough seem to be physical losses of the distinctive features of the cells expressed in the polysaccharide envelope, as though the germ plasm of this organism contained a certain stable nucleus and a variable periphery which may be disposed of altogether. Still more extravagant, and yet conclusively proved, phenomena are enacted if a culture of the rough phase is added to a vaccine consisting of dead cells of the smooth phase with a trace of the antirough serum. For in this case rough reverts to smooth of the same type to which the cells in the vaccine had belonged. Thus, if a small amount of the rough culture derived from the normal (smooth) line of Type II is added to a suspension of smooth cells of Type III devitalized by heating, a smooth line of Type III, not of Type II, is produced. By this method it seems to be possible to convert at least many of the thirty-two types of the pneumococci into many other types. The transformation of the rough into the smooth of the same type from which the rough had been originally derived is, of course, also accomplished by the same method, if a vaccine of that type is used. The vaccines lose their transforming effectiveness after being heated to the boiling point, but cell suspensions heated to 60°C. and subsequently frozen and thawed are effective.

The strains "transformed" from one type into another retain their new properties after cultivation on suitable media or after passage through animal hosts. Hence, they acquire not merely a temporary polysaccharide envelope of a kind different from that which their ancestors have had, but are able to synthesize the new polysaccharide indefinitely. If this transformation is described as a genetic mutation—and it is difficult to avoid so describing it—we are dealing with authentic cases of induction of specific mutations by specific treatments—a feat which geneticists have vainly tried to accomplish in higher organisms. Admittedly, there are many obscurities in the situation which ought to be cleared up. For example, it seems to be unknown whether the transformation affects every cell in the culture or whether only some cells mutate and others are destroyed; whether

¢ Roche 5/15/82

ZSH 5/16/82